

## REMARKS

By the present amendment, claims 23-35 are amended and new claims 36 and 37 are added. Thus, claims 23-37 are pending. No new matter is added as the amended and new claim language is fully supported by the application as filed, including, but not limited to page 4, lines 9-19 and the Example of page 6. Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### **I. Claim Rejections Under 35 USC §112, Second Paragraph**

Claims 23-35 stand rejected under 35 USC §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant addresses each rejection in the order presented in the Office Action.

Claims 23-35 are rejected as allegedly vague for use of the term “characterized in that.” Applicant has deleted this term and replaced it with the term “wherein” as suggested by the Examiner. Withdrawal of this rejection is respectfully requested.

Claims 23-35 are rejected for use of the allegedly vague term “The method of manufacturing.” Per the Examiner’s suggestion, Applicant has deleted this phrase and replaced it with “A process for the preparation” in claim 23 and amended the dependent claims accordingly to replace "method" with "process". Withdrawal of this rejection is respectfully requested.

Claims 23 and 27 stand rejected for typographical errors. In claim 23, the misspelling of "7-ethyl-1,2,6,7-tetrahydrocamptothecin" has been corrected. In claim 27, the misspelling of "sulfoxide" has also been corrected. Withdrawal of these rejections are respectfully requested.

The claim dependencies of claims 30-32 have been corrected; Applicant respectfully requests withdrawal of this ground of rejection.

## II. Claim Rejections Under 35 USC §103

Claims 23-35 stand rejected under 35 USC §103(a) as allegedly being unpatentable over Lin (U.S. Patent No. 7,151,179). The Examiner alleges that "the process described by Lin (see col. 4, lines 7-50) meets all the limitations of instant claims except that Lin carries oxidation at a temperature below 10 degrees C instead of 15-30 degrees C. However, the temperature does not seem to be critical since the process of Lin produces 7-ethyl-10-hydroxy-camptothecin in high yield (90%) unless applicants provide unexpected results of superior yield of their process as compared to the process of Lin." Because the claimed process does possess unexpected advantages and because the claimed reference is not prior art, Applicant respectfully traverses this rejection.

First, Applicant submits that the present methods provide surprising and unexpected results over the cited art and notes that yields are not the only measure of such results. In particular, Applicant draws the Examiner's attention to the amount of acetic acid used in the claimed method versus the cited art. Claim 23 recites the use of 668 to 1,001 mol of acetic acid per 1 mol of 7-ethyl-1,2,6,7-tetrahydrocamptothecin or 1,130 mol per 1 mol of 7-ethyl-1,2,6,7-tetrahydrocamptothecin. This translates to a range of 38.2 ml to 64.6 ml of acetic acid per mmol of the reactant, 7-ethyl-1,2,6,7-tetrahydrocamptothecin. In contrast, the amount of acetic acid employed by the cited reference is only 197 mol per mol of 7-ethyl-1,2,6,7-tetrahydrocamptothecin, which is 11.25 ml per mmol of reactant. Hence, the claimed invention operates at a significantly more dilute solution of acetic acid than the cited reference. Even if the quantity of water used as solvent (11.25 ml/mmol) in the cited method is taken into account, the reaction still fails to reach the dilution levels found in the claimed method.

At the same time, Applicant's reaction is fast, being carried out in only 5 to 30 minutes. While the cited reference does not disclose the total time for the oxidation, previous reports in the scientific literature have utilized much longer time periods such as overnight (see e.g. Wood et al., *J. Org. Chem.* 1995, **60**, 5739-40, previously submitted as reference A45 in the IDS dated September 21, 2007). It is surprising and counterintuitive that Applicant could decrease reactant

concentration of a bimolecular reaction such as the claimed reaction, yet decrease reaction time. Further, as set forth in claim 36, the present method utilizes significantly less oxidant (0.99-1.9 mol per mol of reactant) than the cited method (2.55 mol per mol of reactant). It is also surprising and counterintuitive that the amount of oxidant could be decreased and that the reaction concentration could be decreased, but still result in a fast reaction. Finally, the higher temperature range of the claimed method (see claim 37) is also advantageous as less energy is needed for cooling and heating of the reaction mixture. There is simply no suggestion in the cited art that increasing the amount of acetic acid, and thereby decreasing reactant concentration would allow the use a faster reaction time.

Second, Applicant submits that the cited reference is not citable as prior art to the present application. Applicant draws the Examiner's attention to the declaration of the inventor, Petr Dobrovolny (hereinafter "Declaration") under 37 C.F.R § 1.131. As set forth in the Declaration at paragraphs 2-5, the claimed methods as shown in the accompanying notebook pages were discovered prior to May 12, 2003, the earliest priority date of the Lin reference. Indeed the notebook pages show the actual example set forth on page 5 of the present specification and which embodies each and every claim.

Although, the experiments were carried out in the Czech Republic, Applicant is entitled to rely on these experiments to establish a date of invention under 35 U.S.C. §104. This statutory provision entitles Applicant to rely on activities in a WTO member country. The Czech Republic acceded to the WTO in the year 1995. As set forth in the Declaration, all experiments were performed therein after the year 1995. Hence, Applicant may properly rely on the experiments described in the Declaration to establish the date of the present invention as after 1995 but before May 12, 2003. As such, the evidence shows that the present method was invented prior to Lin and that Lin is not prior art to the present application under any provision of 35 USC §102 and therefore is not prior art under 35 USC §103(a). For this reason and because of the surprising unexpected results obtained with the present method, Applicant respectfully requests withdrawal of this ground of rejection.

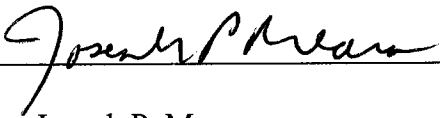
**CONCLUSION**

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. Should any issues remain open after consideration of the present amendment and reply, the Examiner is invited to contact the undersigned so that a prompt disposition of the application may be achieved.

Respectfully submitted,

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